

From the DEPARTMENT OF MOLECULAR MEDICINE AND
SURGERY

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**EARLY ONSET SPINE DEFORMITY.
OUTCOME OF SURGICAL TREATMENT AND
3D MOVEMENT ANALYSIS OF SITTING**

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*They work with herbs
and penicillin
They work with gentleness
and the scalpel.
They dig out the cancer,
close an incision
and say a prayer
to the poverty of the skin.
They are not Gods
though they would like to be;
they are only a human
trying to fix up a human.
Many humans die.
They die like the tender,
palpitating berries
in November.
But all along the doctors remember:
First do no harm.
They would kiss if it would heal.
It would not heal.*

*If the doctors cure
then the sun sees it.
If the doctors kill
then the earth hides it.
The doctors should fear arrogance
more than cardiac arrest.
If they are too proud,
and some are,
then they leave home on horseback
but God returns them on foot.*

Anne Sexton "Doctors"

*To
Kārlis
Ričards
Paula
Marta
and
Dīnija*

ABSTRACT

Early onset, non-idiopathic spine deformities are progressive and associated with increased respiratory and cardiovascular morbidity and mortality as well as neurological and functional deteriorations. If untreated, the deformity progression can continue throughout the adult life and conclude with early mortality mostly due to cardio-pulmonary reason. Wheelchair dependent children with early onset neuropathic and neuromuscular diseases present spine deformities in up to 90%. Abnormal motor control can lead to difficulties in sitting due to postural balance disturbances, spinal deformity, pelvic obliquity and hip disorders.

The aim of this thesis was to analyse a group of patients with early onset non-idiopathic spine deformity from two different perspectives. From clinical perspective: outcome of surgical treatment on multidisciplinary risk patients, the impact of additional neurosurgical intervention in the same surgery session, and the impact of treatment unit when standardizing for pre-operative parameters, surgical technique and surgeon. From functional perspective: the sitting quality was analysed using three-dimensional movement analysis techniques in stationary and dynamic conditions.

Clinical studies. Data from local deformity registry and medical records of consecutive series of patients treated at two departments: one with paediatric multidisciplinary team, and the other with focus on adult spine were included. Variables at base line: age, gender, diagnosis, curve size, type of surgical procedure. The result variables for the group comparisons were as follows: clinical and radiographic outcome, surgery time, length of intensive care and hospital stay, relative blood loss, and occurrence of complications or adverse events.

There was no peri- nor postoperative mortality, no spinal cord damage, no neurological or ambulatory function deterioration. The rate of complications indicating any intervention was 15%. An additional neurosurgical procedure combined with fusion surgery did not increase the complication rate or use of resources compared with fusion surgery alone, except in the length of surgery time. There were statistically significant between-department differences regarding treatment outcome in favour of more specialized department.

3D movement analysis of sitting was performed using two force plates for kinetics and self-reflective markers on anatomical points for kinematics. The analysis was performed during unsupported sitting quiet and when performing circular movements with upper body. Four patients were retested after spine surgery.

The results in both domains showed clear differences between patients with spine deformity when comparing with controls as well as in pre- and postoperative comparisons. During quiet sitting patients were able to compensate deformity and postural control related disequilibrium and keep thorax position similar to controls. During dynamic sitting functional limits of stability were significantly larger in the control group. After the surgery, sitting parameters improved.

Conclusions. Major spine surgery in high risk patients can be performed with safety and good outcome. Impact of organization and work place culture on the outcome might be important and worth further studies. One-stage major spine surgery, even when neurosurgery is included, is safe and does not increase the risk of complications.

The 3D method of movement analysis of quiet sitting and self-initiated sitting movements provides new perspectives to analyse sitting pathology regarding postural balance and symmetry as well as stability in patients with neuropathic and congenital spine deformities. The method enables quantitative intra- and inter-individual comparisons over time and gives a possibility to analyse treatment intervention dependent changes.

SAMMANFATTNING PÅ SVENSKA

Ryggdeformiteter som är medfödda eller orsakas av tidigt i barndomen förekommande neurologiska sjukdomar är som regel progredierande och obehandlade leder till försämrad motorisk funktion samt till hjärt- och lungsjuklighet med förkortad livstid. Uppemot 90% av rullstolsberoende barn med dessa sjukdomar har ryggdeformiteter. Onormal motorisk kontroll kan leda till sittproblem pga störningar i postural balans, stor ryggdeformitet, bäckentippning och höftproblem.

Studiens syfte var att analysera en grupp patienter med en ryggdeformitet, som börjar i tidig barndom, från två olika synvinklar, dels att analysera kliniska operationsresultat och dels funktionella sittandet hos rullstolsberoende. I de kliniska studierna ingick en konsekutiv serie multidisciplinära högrisk-patienter. Man studerade betydelsen av att kombinera en neurokirurgisk intervention vid samma tillfälle med den ortopediska korrektions-operationen i de fall där båda var indicerade. Man jämförde också behandlingsresultaten mellan två behandlande enheter, en med ett multidisciplinärt team modell och en med standard ryggkirurgi modell, i den konsekutiva patientserien, när man hade standardiserat för preoperativa parametrar, kirurgiska tekniker och kirurger. Sittfunktionen studerades både statiskt och dynamiskt med en 3-dimensionell rörelseanalysmetod.

I kliniska studier ingick prospektivt insamlat data från ett lokalt register och från medicinska journaler. Baslinjevariabler var följande: ålder, kön, diagnos, radiologisk deformitetsvinkel, typ av kirurgisk åtgärd. Resultatsvariabler vid gruppjämförelser var följande: kliniska och radiologiska resultat, kirurgitid, antal vård dagar på intensivvårdsavdelningen och i sjukhuset, relativ blodförlust, och förekomst av komplikationer.

Kliniska resultat visade ingen mortalitet, ingen ryggmärgsskada, inga fall med neurologisk eller funktionell försämring. Frekvens av komplikationer som ledde till någon form av åtgärd var 15%. Tillägg av neurokirurgi vid samma operation som den ortopediska deformitetskorrektionen ökade inte komplikationsförekomsten och inte heller resursutnyttjandet fränsett en längre kirurgitid. Det fanns statistiskt signifikanta skillnader i behandlingsresultaten mellan de behandlande enheterna till förmån för den enhet som använde sig av ett multidisciplinärt team och var mer specialiserad för ändamålet. Vid 3-D rörelse-analys av sittandet användes två kraftplattor vid kinetikstudier och självreflekterande markörer på bestämda anatomiska lokaliseringar vid kinematiska studier. Patienten satt dels stilla utan stöd på kraftplattorna och dels gjorde hon en cirkelrörelse med övre kroppen. Fyra patienter analyserades på nytt efter ryggkirurgin.

Signifikanta skillnader fanns mellan patienter med ryggdeformitet och friska kontroller. Resultaten efter operationen visade förbättring jämfört med det preoperativa. Vid stilla sittande kunde patienterna kompensera för deformitets- och postural kontroll relaterade balansstörningar och hålla bröstkorgens position lik den av kontroller. Under dynamiska rörelser var stabilitetsgränserna för sittfunktionen signifikant större hos kontroller än patienter.

Konklusion: Omfattande ryggdeformitetskirurgi – även inkluderande neurokirurgi vid samma operationstillfälle när så indicerad - kan utföras på högriskpatienter med godtagbara risker och goda resultat. Därmed kan man minska resursutnyttjandet, kostnader och rehabiliteringstiden. Organisationen och arbetsplatskulturen är viktiga för resultaten och deras påverkan borde studeras vidare. Studiens 3-D rörelseanalysmetod erbjuder ett sätt att studera sittfunktionen i stilla sittande och dynamiskt både intra- och interindividuell och över tid vid utfallsstudier av kirurgiska interventioner vid behandling av kongenitala och neuropatiska ryggdeformiteter.

LIST OF PUBLICATIONS

This thesis is based on the following publications that will be referred to by their roman numerals:

- I. Murans G, Gustavsson B, Saraste H.
One-stage major spine deformity correction surgery: comparison between groups with and without additional neurosurgical intervention, with more than 24 months of follow-up. Clinical article.
J Neurosurg Spine. 2010; 13:666-671
- II. Murans G, Gustavsson B, Saraste H.
Outcome of major spinal deformity surgery in high-risk patients: comparison between two departments.
Evidence-Based Spine-Care Journal. 2010; Volume 1/Issue 3 11-18
- III. Murans G, Gutierrez-Farewik EM, Saraste H.
Kinematic and kinetic analysis of static sitting of patients with neuropathic spine deformity.
Gait Posture. 2011 Oct; 34(4): 533-8. E-pub 2011 Aug 3.
- IV. Murans G, Gutierrez-Farewik EM, Hirschfeld H, Saraste H.
Quantification of dynamic sitting balance in patients with neuropathic spine deformity.
Submitted for publication

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LIST OF DEFINITIONS

Stability	Behaviour of a system whereby it returns to its equilibrium position after being disturbed. Although stiffness or rigidity of a structure can contribute to its stability, stiffness and stability is not the same thing. When referring to the rigidity of, for example an instrumentation construct, use of the term stiffness or rigidity is more appropriate, not stability ¹ .
Early onset scoliosis	The term was (devised) introduced by Dickson in 1985 ² to define idiopathic spine deformities which start their development before the age of 5 years. Later the term was generalized also for classification of non-idiopathic deformities such as neuromuscular, syndrome related and congenital ³ , which start their development in an early childhood.
Late onset scoliosis	The term devised by Dickson in 1985 ² to define idiopathic spine deformities which starts their development between the age of 6 years and the end of growth maturation of the spine. (The onset of the deformity should not be mixed with the age when the deformity is presented to the medical professional. The two groups are distinct in the prognosis, treatment strategy and morbidity.)
Postural stability	Also referred to as dynamic posturography, is the postural response to an external or volitional perturbation of the postural control system ⁴ or in another words the ability to control the centre of mass projection within the limits of the base of support ⁵ .
Peri-operative relative blood loss	The blood loss during the surgery was calculated relative to the body weight which correlates to the total blood volume of the patient: Relative blood loss= $100 \times \text{blood loss (ml)} / 75 \times \text{weight(kg)}$.

LIST OF ABBREVIATIONS

3D	three dimensional
AP or A+P	anterior and posterior approach for spine surgery in one stage
APN or A+P+N	anterior, posterior and neurosurgical approach for spine surgery in one stage
BOS	base of support
C7	cervical 7 th vertebra
COG	centre of gravity
COM	centre of mass
COP	centre of pressure
EMG	electromyography
FLS	functional limits of stability
FP	force plate
GRF	ground reaction force
H1	hospital 1
H2	hospital 2
ICU	intensive care unit
ITD	inter-trochanteric distance
MMC	myelomeningocele, spina bifida
PBOS	pelvic part of base of support
RA	rheumatoid arthritis
S1	sacral 1st vertebra
SD	standard deviation
SMA	spinal muscular atrophy
VEPTR	vertical expandable prosthetic titanium rib

1 THESIS SUMMARY

1.1 INTRODUCTION

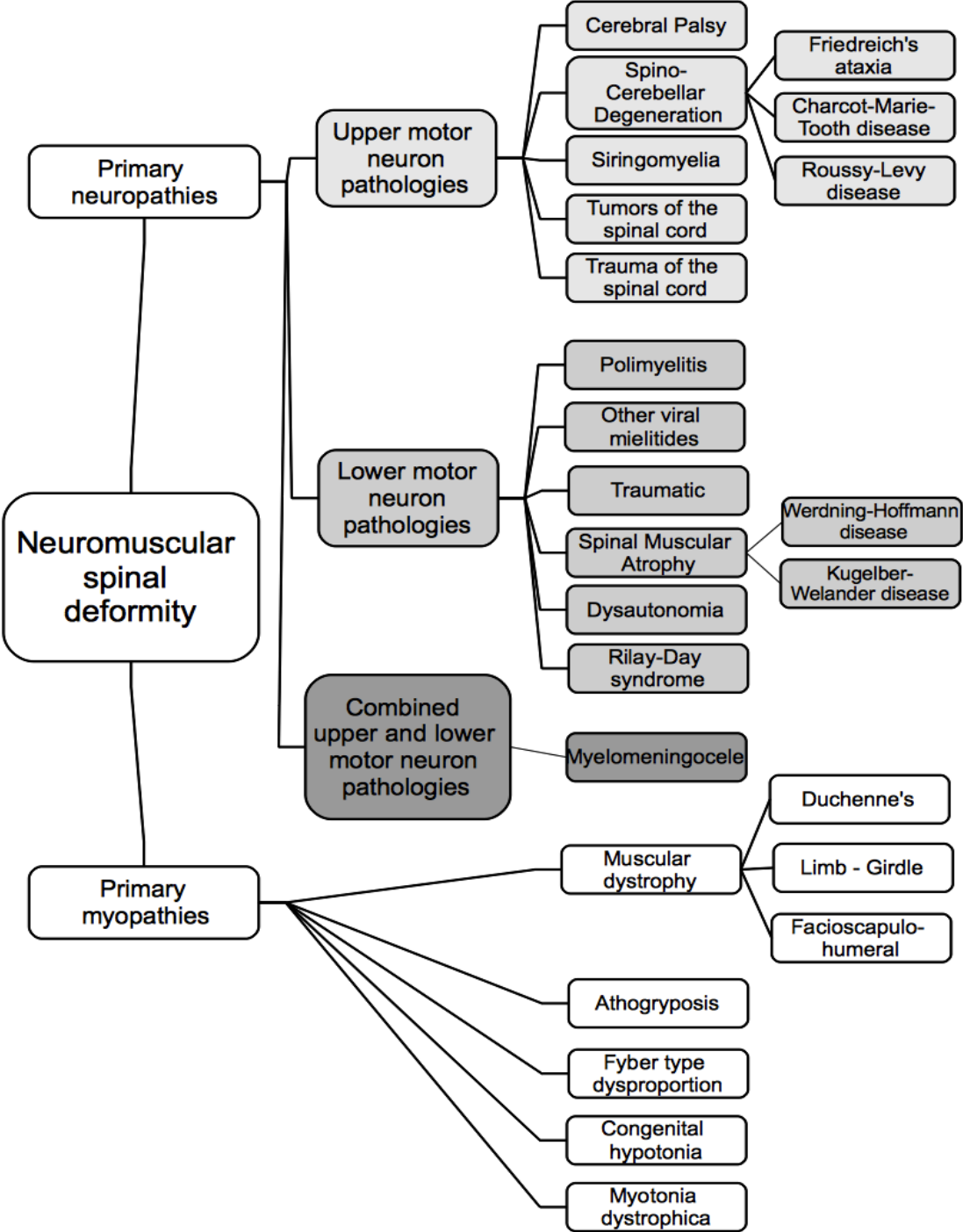
Early onset, non-idiopathic spine deformities are progressive and associated with increased respiratory and cardiovascular morbidity and mortality as well as neurological and functional deteriorations. If untreated, the deformity progression can continue throughout the adult life and conclude with early mortality mostly due to cardio-pulmonar reason.^{2,6-15} Wheelchair dependent children with early onset neuropathic and neuromuscular diseases present with spine deformities in up to 90%.¹⁶⁻¹⁸ In the presence of abnormal motor control, sitting can be difficult due to abnormalities in postural balance, spinal deformity, pelvic abnormal inclination or obliquity and hip pathology¹⁹⁻²¹

The pediatric spine deformities are classified regarding the age of deformity onset and the underlying diagnosis. The classification criteria regarding the age of onset vary. According to the widely used classification of James⁹ the age limits are infantile 0-3 years of age, juvenile 4-9 years and adolescent from 10 years to the end of growth. Dickson in 1985² proposed the use of only two groups based on the fact that only few true juvenile deformities exist and they resemble adolescent type. From the beginning **Early onset scoliosis** was defined as an idiopathic spine deformity, which starts to develop before the age of 5 years. Later the term was generalized to include non-idiopathic deformities such as neuromuscular, syndrome related and congenital³ ones, which start their development in an early childhood. Early onset scoliosis regardless of its aetiology is associated with increased risk of cardiopulmonary morbidity and mortality^{2,6,9}. **Late onset scoliosis** is defined as an idiopathic spine deformity, which is presented from the age of 6 years and to the end of growth maturation of the spine. This term also was later generalized to include non- idiopathic deformities, which are presented later, since they show a more benign course regarding general health and life expectancy^{2,6,9}. The age of onset of the deformity can vary from the age when the deformity is presented for any medical professional.

There is a specialty dependent variation on the use of the term “neuromuscular disease.”²² The SRS (scoliosis research society) classification of neuromuscular spinal deformity is presented in **Figure 1**.

Based on the knowledge of the natural history of early onset spine deformities, a surgical treatment even with explicit comorbidities has rational grounds. When reducing the spine deformity and addressing the associated dysplastic thorax deformity, patients can improve their functional musculoskeletal and cardiopulmonary well-being as well as prolong their lives²³. The treatment of such deformities with non-operative methods has limited potential albeit possessing low complication profile. On the contrary surgical treatment is effective and gives lasting results, but it is associated with high complication rates, more than 50% for instance in patients with spina bifida^{7,24-29}. To reduce costs and risks for complications as well as to evaluate the functional outcome of surgical treatment is essential²³.

Figure 1 Scoliosis Research Society Classification of Neuromuscular Spinal Deformity



1.1.1 Outcome of surgical treatment

The high complication rate can discourage both medical staff and society representatives from justifying surgical treatment of early onset non-idiopathic spine deformities²⁹⁻³². Therefore it is of importance to analyse cohorts of patients treated surgically to create a base for future treatment decisions. To my current knowledge no prospective randomized controlled trials (RCT) on surgical treatment of neuromuscular/neuropathic spine deformities are published. Probable causes are as follows: 1) several diagnosis groups with specific surgical needs; 2) small number of patients; and 3) randomization into an untreated control group are not reasonable due to complex medical problems and many confounding factors, nor ethical due to obvious positive effects of treatment in most diagnosis groups. Observational cohort study design is more aimed for these patient groups^{33,34} and follow-up studies of treatment programs and spine register data can be justified as basis for future treatment decisions.

The responsibility for overall success of the treatment of early onset deformity patients is the success of a team involved including but not limited to: (1) specialists such as neurosurgeon, orthopedic surgeon, anesthesiologist, neurophysiologist, pediatric urologist; (2) nurses; (3) orthotic specialists etc. From an economic-administrative perspective it can be questioned how important the need for highly specialized teams is when health care resources are restricted. Decision-making of administration of spinal care should be based on the same principles as decision-making of treating doctors – based on personal experience and body of evidence from scientific literature^{35,36}.

Early onset, non-idiopathic spine deformities can be caused by intra-spinal anomalies necessitating both neurosurgical and orthopaedic intervention³⁷⁻³⁸. These deformities, besides, being progressive and associated with increased respiratory and cardiovascular morbidity and mortality rates, have potential for neurological and functional deterioration. If untreated, the deformity progression can continue throughout the patient's adulthood.³⁸ In some cases single neurosurgical release or untethering of the spinal cord can prevent progression of the deformity^{7,39-43}; nevertheless, in most cases, complementary spinal deformity reduction and fusion still is necessary³⁹.

It has not been documented whether neurosurgery and deformity correction should be performed in one session or staged. Most commonly, those treatments are performed on separate occasions. However, the surgical approach to intra-spinal anomalies is usually the same as for posterior fusion. Scar tissue formation after repeated surgery decreases the healing capacity of the wound for the second procedure. Intra-spinal re-tethering is described in the literature⁴⁴⁻⁴⁶. Re-tethering following earlier surgeries was also a clinical observation made by the authors of the current study. In fact, there are only a few reasons for a staged surgery strategy, such as concern about excessive surgery time, with consequently increased bleeding and associated hypothetical risks, as well as medico-legal issues regarding possible complications⁴⁷.

1.1.2 3D movement analysis of sitting

An unbalanced sitting can lead to further progression of spinal and pelvic deformities^{16,17}. A balanced spine over a level pelvis with adequate postural stability is the major prerequisite for an independent and stable sitting with upper extremities free for different tasks, thus providing an improved quality of life – the aim for the treatment. Functional results of spine surgery can be less optimal in spite of achieved fusion. Larsson and co-authors⁴⁸ analysed seat loading in 43 neuromuscular patients and found that after surgery a majority of the patients presented frontal plane imbalance, which they compensated with head and neck movements. The authors stress the need to improve evaluation methods.

The interaction of spinal deformity, pelvic obliquity and inclination, hip pathology and postural control should be considered in preoperative analyses and postoperative evaluations of neuromuscular patients. Evaluation methods should be quantitative, reproducible and comparable between institutions, and possible to perform in paediatric population with poor verbal communication and cognitive ability.

Many current clinical assessment methods are semi-quantitative^{49,50}, in some cases questionnaire-based⁵¹. Whether classic radiological measurements of pelvic and spine position correspond to sitting is debatable^{21,51,52}. Pressure distribution analyses of sitting provide important information about zones of increased pressure with risk for developing pressure ulcers⁵²⁻⁵⁵. They also can be used for loading balance analysis^{52,54,55}. It is not clear whether a direct relationship exists between seat loading balance and general balance of the body, since no simultaneous recording of general body alignment has been previously reported. A promising x-ray and pressure distribution analysis combination was proposed by Lafage et al⁵⁶ to provide connection between radiographic alignment and centre of pressure (COP) position in standing. Radiation risk, however, limits the use in paediatric population.

3D movement analysis has been used extensively in sitting research with different protocols for kinematic, kinetic and EMG recordings⁵⁷⁻⁶⁰. In spite of this, there is lack of studies analysing paediatric patients with neuropathic spine deformities, patients who often have cognitive abnormalities (see for example^{61,62}). 3D analysis could help overcome some inherent problems with a complex subjective assessment based on opinions of parents and/or caregivers, and enable comparisons over time and between subjects. Benefits would be: (1) no exposure to ionizing radiation, (2) quantifiable and three-dimensional description of the posture and loading, (3) low measurement error of marker trajectory data, (4) possible to use on persons with poor ability to verbal communicate.

It is of interest to look both at stationary sitting balance as well as at dynamic sitting, representing different domains of the equilibrium system.

1.1.2.1 Static assessment

Hypothetically 3D kinematic and kinetic analyses of quiet sitting using a 3D motion analysis system and two force plates would make it possible to study quantitative body alignment as well as seat loading and symmetry including Centre of Gravity (COG) trajectory assessment.

1.1.2.2 *Dynamic stability assessment*

The functional independence of non-ambulators relies on postural stability in sitting and on maintaining erect body alignment to provide functional head and arm positions. In biomechanics stability means that a system returns to equilibrium after a perturbation⁶³. Postural stability, also referred to as dynamic posturography, is the postural response to an external or volitional perturbation of the postural control system⁴. Postural stability/balance is also referred to as the ability to control the centre of mass projection within the limits of BOS⁵. The control of centre of mass movements is implemented through the postural control system. The action of the postural control system is carried out by interaction with BOS, and can be recorded directly by a force plate as Ground Reaction Force (GRF) at the Centre of Pressure (COP)^{5,64}. The COP position data are used widely for balance analyses as a measure of the postural control system's action⁶⁵⁻⁶⁸.

For healthy subjects stability demands are low when sitting, since the base of support is large. In non-ambulatory patients with neuropathic diseases, e.g. in conditions such as CP⁶⁹, spina bifida⁷⁰, muscular dystrophies, neuroendocrine syndromes^{71,72}, the postural control system itself is deficient. These conditions predispose to severe spine deformities, which deteriorate sitting stability^{55,73-75}. There are very few quantitative studies on the role of surgical and/or orthotic treatments to improve the postural alignment in neuropathic spine deformities^{23,76-79}.

After treatment to straighten the spine and level the pelvis, improvements in symmetry and sitting support area have been documented in static conditions captured by x-ray and pressure distribution technique and with movement analysis⁸⁰. A well balanced, reduced and fused spine should prevent muscle fatigue in sitting, create better prerequisites for hand function, and improve the base of sitting support area with decreased risk for decubitus^{19,81,82}. The possible improvements have yet to be proven in dynamic conditions.

In persons with neuromuscular disorders, postural disturbances are augmented by voluntary movements of upper body such as leaning in any direction^{65,69,73,75}. Static measurements are then of poor value, since the COM must be controlled dynamically. Consequently, motion during sitting is an important domain of balance analysis.

The major consideration when measuring the postural stability is to acquire the limits of stability or functional limits of stability (FLS)⁶⁸. A quantitative method to monitor a relative size of self-induced perturbations in different forms (reaching, upper body circular movements etc.) would enable comparisons over time and between subjects. The larger the FLS is relative to BOS, the better is the dynamic postural stability of the subject. Use of a movement analysis system consisting of force plates and kinematic recording techniques are considered one of the best options to measure FLS^{66,83}. This method has been used to analyse different aspects of sitting, such as postural control of scoliosis, wheelchair propulsion, and transferring from bed to chair^{84,85}.

Earlier publications on balance analyses depict two basic ways to look at the problem^{4,5,65,68,69,83}. One way is to measure the range and symmetry of the upper body movements regarding area of the base of support. The other looks at excursions of the COP during dynamic tasks in terms of symmetry and area. An additional method studies loading patterns of parallel force plates⁸⁰ similarly to measurements used in seat load analyses with a pressure mat^{55,73,74,83}. To study the variability of sitting asymmetry by loading /unloading patterns between right and left sides

might capture a subject's ability to transfer weight between sides and consequently monitor dynamic stability.

However, these methods have rarely been applied on treatment outcome in neuropathic spine deformities, a patient group with major problems in sitting and activities of daily living.

1.2 AIMS OF THE INVESTIGATIONS

1.2.1 Study I

The aim was to study complex spine deformity cases, in which both neurosurgical interventions and deformity corrections were indicated. In specific, the aim was to analyze, if an additional neurosurgical procedure in the same session with a combined anterior and posterior deformity correction increased peri- and post-operative morbidity and mortality in comparison to one stage combined anterior and posterior deformity surgery in patients without neurosurgery.

1.2.2 Study II

To study outcome, resource use, and complications in pediatric high risk spine deformity surgery, and to compare two departments: H1 with pediatric multidisciplinary team and H2 with focus on adult spine.

1.2.3 Study III

The aim was to validate a 3D method to analyse quiet sitting in paediatric patients with neuropathic and congenital spine deformities and in a control population.

The specific aims were:

- To test whether the method can describe quiet sitting and its pathology in the patient cohort.
- To describe differences between patients and age- and weight-matched controls.
- To apply the method for a pre- and post-operative comparison in a patient subgroup to analyse possible surgery-related changes in sitting.

1.2.4 Study IV

The aim was to validate a method to analyse dynamic balance in sitting with a movement analysis system in paediatric patients with neuropathic and congenital spine deformities and in a control population.

The specific aims were:

- To test whether the method can describe dynamic sitting balance during voluntary postural changes, and differences between patients and age- and weight-matched controls.
- To apply the method pre- and post-operatively to capture possible surgery-related changes in dynamic sitting balance.

1.3 PARTICIPANTS

1.3.1 Study I

A consecutive series of 81 patient with rigid and large spine deformities indicating a combined anterior and posterior deformity correction surgery according to the current treatment program were included in the study. All deformity surgeries were performed by one and the same orthopaedic spine surgeon as a combined procedure in one surgical session in 1997-2004. In 24 cases out of 81 there were additional intraspinal pathologies indicating a neurosurgical procedure. The intraspinal pathology was judged to have an impact on deformity progression and on neurological clinical findings. The neurosurgery was performed by one neurosurgeon or under his supervision in the very same session as the combined one-stage deformity surgery in co-operation with the orthopaedic surgeon. The intraspinal pathologies and neurosurgical procedures are listed in Table 1.

Table 1 Age at surgery, diagnosis, in addition to scoliosis, indication for neurosurgery, and procedures performed in 24 patients with spine deformity correction plus additional neurosurgery *

Case No	Age at Op (Yrs.)	Diagnosis/Entity	Neurosurgical Procedure	Levels of anterior fusion	Levels of posterior fusion
1	11	MMC, TLT	TLU	T12-L4	T4-S1
2	10	MMC, RA, thoracolumbar re-tethering	TLU	T4-S1	T4-S1
3	15	MMC, diastematomyelia	TLU, spur excision	T10-L5	T4-L5
4	13	MMC, placode, TLR	TLU	T9-L3	T4-S1
5	12	MMC, placode, dermoid cysta, thoracolumbar re-tethering	TLU	T12-L4	T4-L5
6	9	MMC, diastematomyelia	TLU, spur excision	T5-L1	T4-S1
7	5	MMC, diastematomyelia	TLU, spur excision	L2-S1	L2-Pelvis
8	13	Achondroplasia deformans	TLU	T7-L3	T6-L5
9	12	Congenital scoliosis, diastematomyelia, thoracolumbar retethering	TLU, spur excision	L1-L4	T10-L1
10	1	MMC, kyphosis, retethering, pseudarthrosis	thoraco-lumbo-sacral untethering	T7-L3	T6-L5
11	14	Congenital scoliosis, intraspinal lipoma, tethered filum terminale.	sacro-lumbar untethering, tumor exstirpation	T10-L2	T6-L4
12	7	MMC, spinal tumor	TLU, tumor exstirpation	T9-L5	T4-S1
13	6	MMC, intradural anomalies	TLU	T10-L3	T3-L5
14	3	MMC, kyphosis, thoracolumbar tethering	TLU	T11-S1	T4-S2
15	8	MMC, TLR	TLU	T10-L3	T3-L5
16	32	Diastematomyelia	TLU, spur excision	T12-L3	T6-S1
17	10	MMC, retethering	TLU	L1-L5	T4-S1
18	2	MMC, kyphosis, thoracolumbar tethering	TLU	T12-L3	T6-S1
19	9	Lumbosacral agenesis, diastematomyelia	lumbar untethering	T12-L5(T2-S1
20	4	MMC, kyphosis, TLT	TLU	T12-L4	T4-Pelvis
21	6	MMC, medulla atrophy, tethered filum terminale	TLU	L2-L4	L1-L4
22	3	MMC, TLT	TLU	T6-Th12	T4-S1
23	2	Kongenital stenosis, Cysta, tethered filum terminale	thoracic untethering	T9-Th12	T5-L3
24	2	MMC, kyphosis, tethering	TLU	N/A	T10-Pelvis
Mea	8.71				
n±	± 6.6				
SD					

* MMC = myelomeningocele; NA = not applicable; RA = rheumatoid arthritis; TLR = thoracolumbar retethering; TLT = TL tethering; TLU = TL untethering.

† All myelomeningoceles had been treated in the neonatal period with closing of the defect.

The data were captured from the medical records and the unit's spine deformity register. The follow-up time varied from 24 to 104 months, mean 31 months.

The distribution of the patients according to the diagnosis, age and weight is listed in **Table 2**. The ages of the patients at surgery varied from 1 to 32 years. The distribution according to the functional ambulation was as follows: 14 normal ambulators with clinically intact neurology, 6 ambulators with some neuropathology, 11 ambulators with orthoses or walking aids, 50 wheelchair-dependents.

There were no statistically significant differences between the groups with (APN) and without (AP) neurosurgery regarding the baseline data, such as weight, gender, type and degree of deformity, neither regarding the distribution of deformity correction procedures (length of the fusion, caudal fixation level) nor the correction outcome. However there were significant between-group differences regarding diagnosis and patient age, both of which are related to indications for neurosurgery. Myelomeningocele (MMC) patients composed a majority of APN group. All included MMC patients had been treated with the primary closure in the neonatal period. Some of them had been surgically treated for tethering later on again but before the present condition with recurrence of symptom giving retethering. They are marked "retethering" in Table 1.

Table 2 The distribution of the patients according to diagnosis, age and weight in the study groups*

	Study groups		Total (n=81)
	A+P (n=57)	A+P+N (n=24)	
Age median (\pm SD)	11 (\pm 5.23)	8.7 (\pm 6.6)	11 (\pm 5.82)
Weight median (\pm SD)	30 (\pm 9.8)	22.5 (\pm 14.2)	28 (\pm 11.6)
Sex M/F	32/25	9/15	41/40
Functional capacity			
normal ambulator	12	2	14
ambulator with some neuropathology	4	2	6
ambulator with orthoses/walking aids	9	2	11
wheelchair	32	18	50
Deformity related diagnosis			
myelomeningocele	4	18	22
cerebral palsy	24	0	24
spinal muscular atrophy	4	0	4
neuroendocrine syndrome	6	0	6
congenital bone anomaly	11	5	16
tumor, other disease	8	1	9

AP = combined antero-posterior deformity surgery, APN = AP with added on neurosurgery

1.3.2 Study II

Inclusion criteria: Surgically treated patients with congenital and neuromuscular progressive spine deformities.

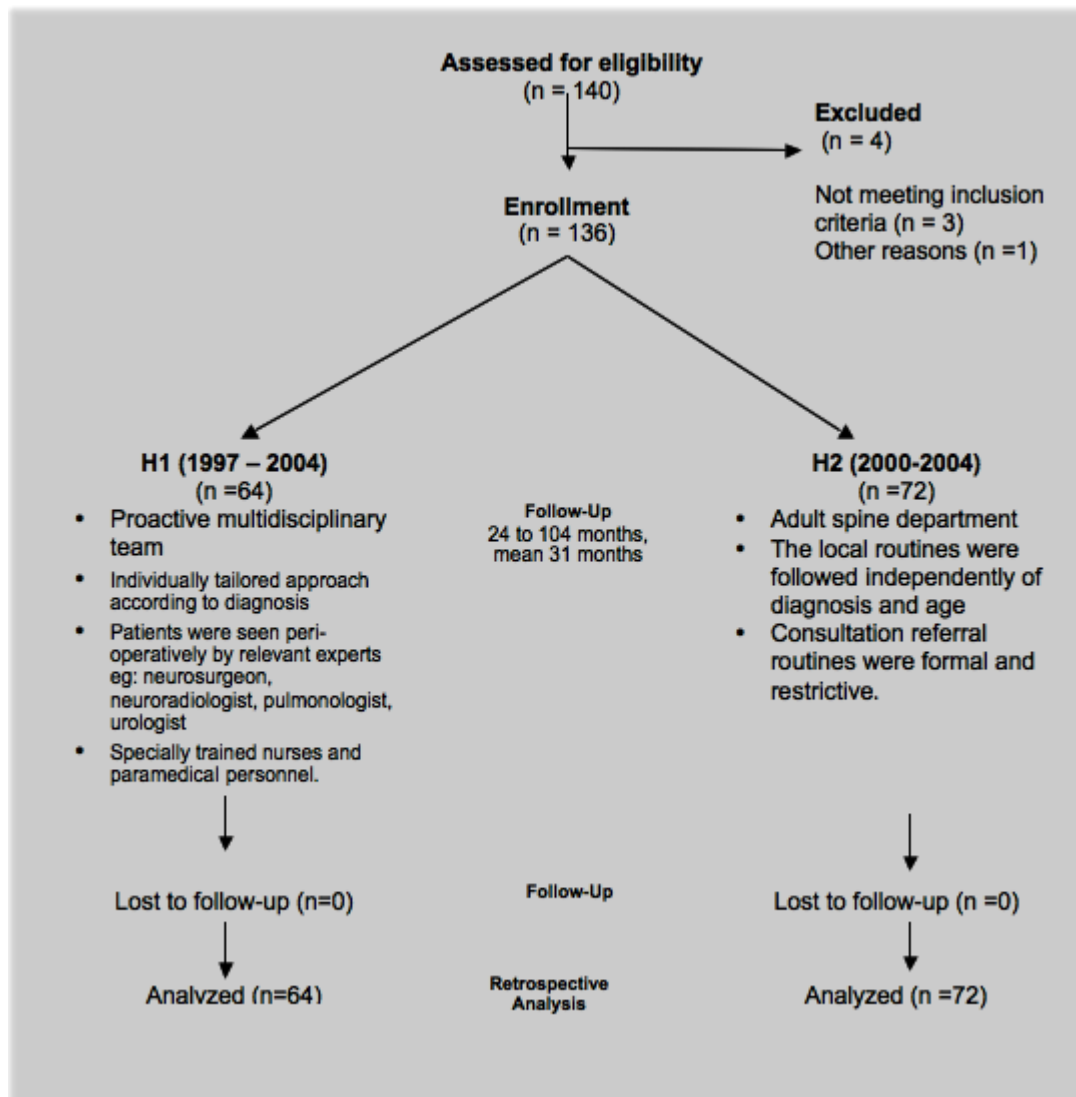
Procedures included : segmental fixation (anterior and/or posterior) and fusion with an additional neurosurgery in the same session if indicated.

Exclusion criteria: Patients with idiopathic spine deformities;

Other than fusion techniques, for instance “VEPTR” and “Growing Rod”;

Patient population and interventions compared (Figure 2) :

Figure 2 Demographic and baseline characteristics of the groups



Prospectively captured data from deformity registry and medical records before and after surgery and at two or more years follow-up on 136 consecutive, surgically treated by one surgeon in two departments: H1 with paediatric multidisciplinary team (1997-2004), and H2 with focus on adult spine (2000-2004). The patient distribution to departments was not by surgeon choice but administrative.

1.3.3 Study III and IV

1.3.3.1 Participants

A consecutive series of 14 children and young adults with a mean age of 12.4, equal gender distribution with neuromuscular and spine deformity, able to sit independently for at least 10 seconds and scheduled for spine deformity surgery were included in study III. Ten out of these were available for study IV. Independent sitting was defined as ability to sit without using arms for support, with unsupported feet and back and without a brace. The examination was included in the routine preoperative examination made by a physiotherapist. The participants could opt for their data to be excluded from this study. Age, gender, diagnosis, radiographic apex and Cobb angle of the major curve as well as pelvic obliquity in frontal plane in degrees are shown in Table 3. Four patients were unable to tolerate marker placement since sitting longevity was short. Four patients were retested after the spine surgery. Ten age-matched normal controls were included in the study.

Table 3 Data of patients included in studies III and IV. Data of Cobb angles of spine deformity and pelvic obliquity were obtained by standard x-ray technique *

Case No.	Age (Yrs)	Sex	Study IV	Post Op	Diagnosis	Apex	Cobb Angle	Convex	Pelvic obl.	Lower side of pelvis
1	8	M	Y	Y	Spina bifida	L1	56°	Right	0°	-
2	4	M	Y	N	NES	T12	70°	Right	0°	-
3	13	M	Y	N	NES	T5	53°	Right	10°	left
4	4	F	Y	Y	Congenital Spine deformity	L2	40°	left	25°	left
5	11	F	Y	Y	Spina bifida	L1	65°	left	20°	left
6	12	M	Y	Y	Spina bifida, kyfoscoliosis	T10 KY=L2	80°	right	20°	right
7	10	F	Y	N	Spina bifida + JRA	T8	85°	left	10°	left
8	19	F	Y	N	Congenital kyphosis	T7	KY=100°	--	0°	--
9	14	M	Y	N	NES	T8	60°	Right	17°	left
10	14	F	N	N	CP	L2	65°	left	32°	left
11	11	M	N	N	Spina bifida	L2	70°	left	25°	left
12	13	F	N	N	Aikordie syndrome	T8	110°	left	20°	left
13	24	M	Y	N	Spina bifida, lordoscoliosis	L3	SC =40° LO=90°	left	10°	left
14	15	F	N	N	NES	L1	70°	--	0°	--

* NES = neuroendocrine syndrome related spine deformity; KY = kyphosis; LO = lordosis; SC = scoliosis; JRA- Juvenile Rheumatoid Arthritis; CP- Cerebral Palsy; Y =yes; N=no;

1.4 METHODS

1.4.1 Study I and II

1.4.1.1 Outcome data

The following data from the retrospective cohort study were included:

- Clinical and neurological status and functional ambulation, radiographically measured deformity angles and spine balance before and after surgery and at follow-up were recorded in the deformity registry at the time of each examination by the surgeon. The follow-up recordings and counter-checking to medical reports were performed by the first author, who did not treat the patients.
- Surgery time, intensive care department (ICU) stay, and hospitalization time.
- Occurrence of complications or adverse events. The complications were recorded as follows:
 - peri-operative occurrence of spinal cord damage, dural tear, implant failure, fracture, anesthesiologic problems and other adverse events;
 - postoperative wound infections, occurrence of neurological deterioration, implant problems, respiratory problems, urinary tract infection, thrombosis, anesthesiological problems and other adverse events;
 - late occurrence of neurological deterioration, infection, pseudarthrosis, implant problems, progression of deformity, pain, pressure sores and other adverse events.
 - Complications were divided into major and minor categories.
 - Minor complications did not impair the hospital course nor the result of the surgery neither did they indicate any surgical or other intervention.
 - Major complications were all other events which altered the hospital course, indicated any additional surgical treatment or affected the final surgical outcome of the patient.
 - A more detailed analysis was carried out regarding all infections and hospital related complications.
 - The hospital related complications were events not related to surgical procedures or implants.

1.4.1.2 Surgical technique

Before the surgery, the patients were optimized regarding the nutritional and cardiovascular status, and respiratory function. Prophylactic antibiotics were used only during surgery.

The deformity surgery included either a posterior or a one-stage combined anterior and posterior procedure depending on the rigidity and size of the curve and the age of the patient according to the current treatment program. The deformity surgery included combined anterior and posterior procedures. The anterior procedure included a retroperitoneal and/or transthoracic approach with no or minimal incision through the diaphragm. Segmental vessels were principally not sacrificed. The anterior fusion included discectomies, autologous rib or crista bone transplantation mainly without implants or with titanium one-rod segmental fixation system, which was used in two cases.

The posterior approach consisted of segmental fixation with titanium implants. Both hooks and screws, occasionally combined with wires, were used. Autologous or homologous bone,

occasionally combined with bone substitute, were used for posterior fusion.

A neurosurgical intervention was performed in the same session if indicated due to intraspinal findings and neurological symptoms preoperatively. The neurosurgery included procedures to untether spinal cord, excise/resect tumors, other expansive processes, adhesences, or malformations like bone spurs in diastematomyelia. Interventions directly related to Chiari-malformation, such as occipito-cervical decompression, or shunt problems were not performed in the same session as the deformity correction. Thus, these procedures were not included in the current project.

There were furthermore no cases with dural sac transection for paralytic kyphosis surgery, since this procedure was discontinued before the current project started. During the study period the dural sac was saved also at vertebral resections, inspite of this technique being more demanding regarding dissection technique and implant choice.

1.4.2 Study III and IV

1.4.2.1 *Equipment and test procedure*

Two AMTI force plates (type MC818, size 203 mm×457 mm, Advanced Mechanical Technology Inc., Newton, Massachusetts, USA) were mounted on a height-adjustable bench. The participants were instructed to sit as far back as possible and the bench height was adjusted such that the participants' feet were approximately 100 mm above the floor. The kinetic recordings were performed by one and the same examiner synchronously with kinematic data from "Elite" (BTS S.p.A, Italy) motion analysis system consisting of 6 cameras for capturing 3D coordinates of reflective markers in synchronous collection at 100 Hz. Two recording sessions were performed:

1.4.2.1.1 Study III

Participants were instructed to sit in a position as close to their normal sitting posture as possible, to place their arms crossed on their chests and to look straight ahead. Ten seconds of quiet sitting was recorded in synchronous collection by force plates and motion analysis at 100 Hz.

1.4.2.1.2 Study IV

After taking a quiet sitting position as normal and stable as possible, subjects were instructed to perform upper body excursions starting with leaning forward as much as possible without upsetting equilibrium. Then this movement was continued by a circular upper body excursion through maximal leaning laterally, backwards and laterally to the other side, and then forward again. One trial was performed in 30 seconds with multiple rounds. One cycle was defined between two maximum forward leanings. The data of each cycle were normalized to percent of the measurement cycle.

The raw data were captured and tracked by standard software of the hardware manufacturer. The particular segment angle and segment position analyses, and force plate data analyses were performed by “Visual 3D”(C-Motion, Inc. USA) and “Matlab” (Math Works, USA) software. Measurements were performed 0–3 months before the scheduled surgery as a part of the routine preoperative clinical examination and 3–6 months after surgery.

Reflective markers were attached to anatomical landmarks as follows: thoraco-abdominal segment was identified by markers on each acromio-clavicular joint, on spinous process of 7th cervical vertebra (C7), and on spinous process of 10th thoracic vertebra (Th10). Pelvis was identified by markers localized on the top of each iliac crest and one marker on spinous process of the first sacral vertebra (S1). Additional markers were placed on both greater trochanters. The head segment was identified by two markers localized on the each temple and one over occipital area.

The pelvic part of base of support (PBOS) was defined using S1 and both trochanteric marker 3D positions by calculating the area of the triangle formed by them.

1.4.2.2 Description of measurements used in the study

1.4.2.2.1 Study III

1.4.2.2.1.1 Position of pelvis:

Obliquity, tilt and rotation (in Cardan angles) of pelvis segments (Figure 3/a) were calculated relative to the global coordinate system of the lab. Angles were defined as follows: obliquity = rotation around x axis (positive value in the direction to the right); pelvic tilt = rotation around Z (medial-lateral) axis (positive value when going into flexion); pelvic rotation = rotation around Y (vertical) axis (positive value in rotation to the right);

1.4.2.2.1.2 Position of thorax-shoulder segment

flexion, lateral bending, rotation (in Cardan angles) of thorax segment (Figure 3/a) was calculated relative to global coordinate system of the lab. Angles were defined as follows: lateral bending = rotation around X axis (positive value in direction to the right); thoracic flexion = rotation around Z axis (positive value when going into flexion); thoracic rotation = rotation around Y axis (positive value if rotation to the right).

1.4.2.2.1.3 The plumb line of C7 over S1

The plumb line of C7 over S1 (comparable with the radiographic C7 - S1) in sagittal (Dx), coronal (Dz), and transverse planes (not shown in the figure) (Figure 3/c) was calculated. The geometric centre of triangle formed by both acromio-clavicular and C7 markers for the thoracic segment was used as a substitute to upper point of the plumb line, and a geometric centre of both iliac crista markers and S1 for the pelvis segment was used as substitute for reference point of the plumb line. Transverse plane, i.e. rotation, data was calculated as relative Cardan angle between thoracic and pelvic segments in transverse plane.

1.4.2.2.1.4 Seat load asymmetry

Use of 2 force plates to measure Reaction Force (RF) vectors at the point of Centre of Pressure (COP, A and B in the Figure 3/b) Ground Reaction Force of the left FP (GRF1_{vert}) and Ground Reaction Force of the right FP GRF2_{vert} respectively, as well as overall resultant RF -

GRF_TOT_{vert} (point C in Figure 3/ b). The absolute asymmetry index relative to overall resultant GRF_TOT_{vert} in percent was calculated using the formula shown below. A perfect symmetry equals 0%, total asymmetry equals 100% (Equation 1):

$$\text{Index}_{\text{asym}} = \text{Abs}(\text{GRF1}_{\text{vert}} - \text{GRF2}_{\text{vert}}) / \text{GRF_TOT}_{\text{vert}} \times 100 \quad (1)$$

1.4.2.2.1.5 COP position symmetry

Absolute angle β of asymmetry formed by points of COP position on each force plate relative to the medial-lateral axis was calculated. $\beta=0^\circ$ means a perfect symmetry meaning that COP from both force plates lies on the line parallel to Z axis (Figure 3/b) With increasing β -values the line connecting COP of both sides becomes more oblique, which indicates increasing asymmetry;

1.4.2.2.1.6 Common COP position and symmetry

The position of inter-trochanteric midpoint relative to the common COP (combined data from both force plates) and symmetry in anterior-posterior (S_{AP} , Figure 3/d) and medial-lateral directions (S_{ML} , Figure 3/d). The anterior-posterior location (S_{AP}) is calculated in percent relative to inter-trochanteric distance (ITD) acquired from marker data of left and right femoral major trochanters. The COP location anterior to the inter-trochanteric line is considered as positive value (+ D_{AP}) and posterior as a negative value (- D_{AP}). (Equation 2):

$$S_{AP} (\%) = D_{AP} / \text{ITD} \times 100 \quad (2)$$

The medial-lateral location of the COP also was calculated relative to trochanteric markers. The absolute deviation distance of the COP from the midpoint of intertrochanteric line was measured (D_{ML}) and relative medial-lateral asymmetry S_{ML} relative to ITD was calculated (Equation 3):

$$S_{ML} (\%) = D_{ML} / \text{ITD} \times 100 \quad (3)$$

1.4.2.2.2 Study IV

1.4.2.2.2.1 FLS of upper body and head

To measure the FLS of upper body movements, the trajectories shaped by head and thoracic segment centres were captured in the transverse plane. The centres of segments for trajectory analysis were acquired by creating a virtual marker in the centre of triangle formed by three markers on each segment (**Figure 4/A**). The positional centroid of trajectories was found by calculating the mean values of the trajectory data in anterior-posterior (AP) and medial-lateral (ML) direction. The area of trajectories was calculated in per cent relative to the area of PBOS (**Figure 4/B**).

1.4.2.2.2.2 FLS of COP

To measure the FLS of the COP, the position of common COP was calculated using COP data from each side, collected by the two force plates. The area of COP trajectory (ACOP) was normalized to the PBOS.

1.4.2.2.2.3 COP positional centroid symmetry

The positional centroid of COP trajectory was calculated and its relationship to intertrochanteric midpoint was defined as asymmetry index relative to inter-trochanteric distance (ITD). The anterior-posterior location of COP positional centroid point (S_{AP}) was calculated in percentage of

inter-trochanteric distance acquired from marker data of left and right femoral major trochanters. The COP location anterior to the inter-trochanteric line is considered as positive value (+ S_{AP}) and the posterior one as a negative value (- S_{AP}). The medial-lateral location of the COP was calculated relative to the trochanteric markers. The absolute deviation distance of the COP from the midpoint of intertrochanteric line (S_{ML}) was measured, and the relative medial-lateral asymmetry (S_{ML}) was calculated relative to ITD (**Figure 4/B**).

1.4.2.2.2.4 Loading and unloading difference between FP1 and FP 2

The ability of the patient to transfer weight between sides during circular movements over the cycle was calculated by obtaining the range between maximum loading of one force plate and minimum loading of opposite platform in per cent of body weight (BW). The range was calculated as index of loading/unloading difference (Equation 4) to measure the stability. The difference between average loadings of both force plates was calculated as symmetry index (**Figure 4/C**).

$$\text{INDEX}_{\text{load/unload}} = (\text{LoadMAX}_{\text{FP1}} - \text{LoadMIN}_{\text{FP2}} + \text{LoadMAX}_{\text{FP2}} - \text{LoadMIN}_{\text{FP1}}) / 2 / \text{BW} \quad (4)$$

1.4.3 Statistical analysis

For all studies statistically significant difference was set to $p \leq 0.05$ and analysis was performed using SPSS software.

1.4.3.1 Study I

For statistical analysis, within-group comparisons such tests were performed as the ANOVA, Pearson, chi-square, and Fisher exact test where appropriate.

1.4.3.2 Study II

Statistical significance of comparison between H1 and H2 regarding outcome variables were calculated using multiple logistic regression to adjust for the baseline differences.

1.4.3.3 Study III and IV

Due to small number of participants only non-parametric tests were used. For continuous variables Mann-Whitney test was used. For correlation analysis Spearman coefficient of association (r) was calculated. Strong association was considerate with $r > 0.8$, moderate association with $r > 0.5$

Figure 3 (a) Coordinates of markers at anatomically important points were used to define position of the pelvis segment: obliquity, tilt, rotation, and position of thorax-shoulder complex: flexion, lateral bending, rotation. (b) The schematic presentation of seat load symmetry and angle β , see explanations in the text. (c) The plumb line of C7 over S1 measured in sagittal (Dx), coronal (Dz), and transverse planes (data calculated as relative angle between thorax-shoulder complex and pelvis segments in transverse plane). (d) Combined COP position and symmetry in anterior-posterior (S_{AP}) and medial-lateral directions (S_{ML}) relative to intertrochanteric line.

Anatomically important points: RIC- right iliac crest, LIC - left iliac crest, S1- spinous process of the first sacral segment, ACR – acromio-clavicular joint of the right side, ACL - acromio-clavicular joint of the left side, C7 – spinous process of the 7th cervical vertebra.

1.4.3.4

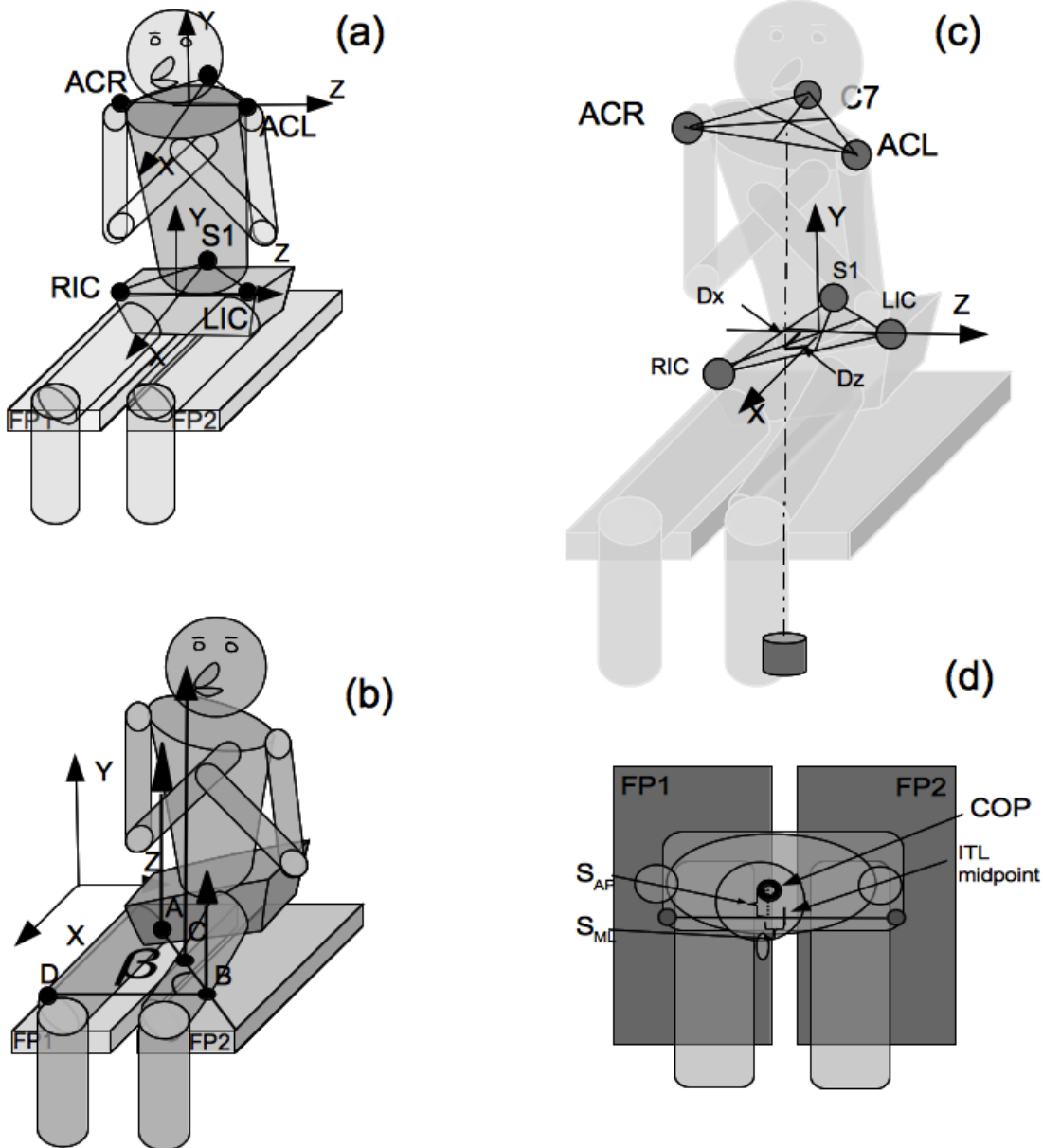
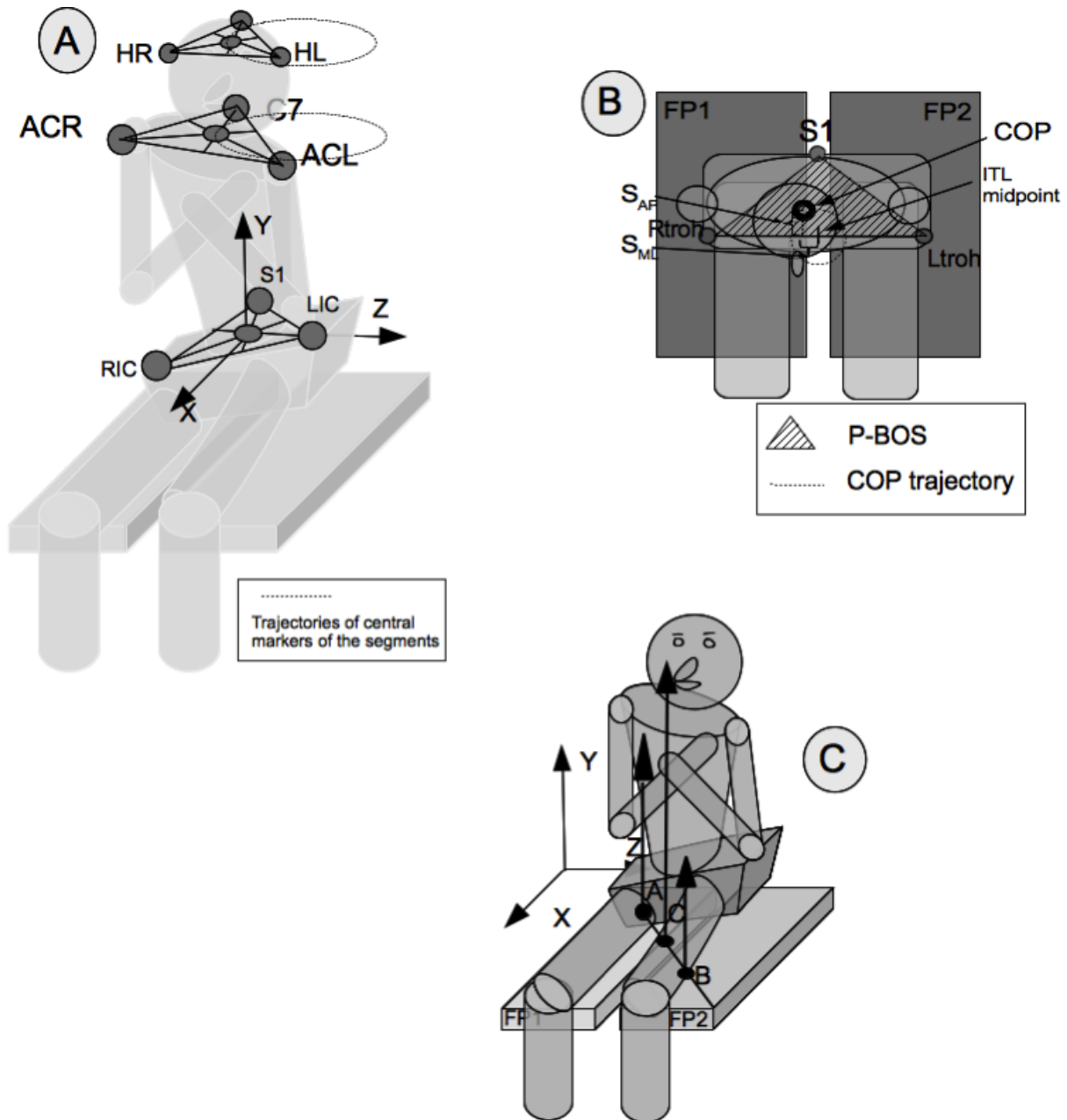


Figure 4 (A) To measure the FLS the trajectories shaped by head and thoracic segment centres were captured in the transverse plane. The centres of segments for trajectory analysis were acquired by creating a virtual marker in the centre of triangle formed by three markers on each segment. (B) COP trajectory analysis relative to PBOS regarding area and symmetry of positional centroid in anterior-posterior (S_{AP}) and medial-lateral directions (S_{ML}) relative to intertrochanteric line. (C) The schematic presentation of seat load analysis.

Anatomically important points: **RIC**- right iliac crest, **LIC** - left iliac crest, **S1**- spinous process of the first sacral segment, **ACR** – acromio-clavicular joint of the right side, **ACL** - acromio-clavicular joint of the left side, **C7** – spinous process of the 7th cervical vertebra. **FP** – force plate **PBOS** - pelvic part of base of support



1.5 RESULTS

1.5.1 Study I

The mean \pm SD of the radiographic variables before and after surgery and at follow-up, as well as the deformity correction percentages for whole study group are given in Table 4. The average correction of Cobb angle was 56.7%. The loss of correction during the follow-up was minor, in average 3 degrees. The mean correction of pelvic obliquity was 74.7% with a minor loss of correction during the follow-up, 0.8 degrees in average.

A comparison between the groups without and with neurosurgery showed a significantly longer surgery time when neurosurgery was included, as expected, 568 (\pm 150.8) and 690 (\pm 170.2) minutes, respectively. The time to change the patient's position is included. No other statistically significant between group differences in the studied variables were found (Table 5).

The average relative blood loss was 77% (SD=45) with a range from 15 to 235 %. Cell-Saver was used in 44 cases, with no statistical difference between groups. To add on the neurosurgical procedure in the same stage did not significantly increase the blood loss.

There was no per- nor postoperative mortality, nor any case with spinal cord damage or early or late neurological deterioration. The ambulatory function did not deteriorate in any case.

To add on the neurosurgical procedure at the same stage showed no significantly negative impact on the risk for complications. The rate of complications, which rendered to any additional intervention was 12.3%. Their distribution is presented in Table 6. Minor complications or rather adverse events not needing any intervention and without any impact on the outcome occurred in 18 (22%) cases.

Variable	Preop value (°)	FU value (°)
Cobb	61.2 \pm 32. 7	29.4 \pm 22. 1
rotation	25.3 \pm 21. 1	12.25 \pm 1 5.3
thoracic kyphosis	28.2 \pm 33. 9	29 \pm 16.4
lumbar lordosis	24.6 \pm 50	33.5 \pm 19. 4
pelvic obliquity	11.5 \pm 14. 4	3.7 \pm 7.5

Table 4 Mean \pm SD of radiographic variables before and at follow-up (FU).

Table 5 Comparison between combined anterior and posterior (A+P) and A+P with additional neurosurgery (A+P+N) groups. Values are given as the mean \pm SD. Except the surgery time, the differences were not statistically significant.

Parameter	A+P	A+P+N
Number of patients	57	24
Op time (min)	568 \pm 151.8	690 \pm 170
ICU stay (days)	1.94 \pm 2.3	2.92 \pm 3.7
Hospital stay (days)	11.2 \pm 8.5	13.7 \pm 6.2
Relative blood loss (%)	79.7 \pm 47.1	71.3 \pm 43.6
Correction of Cobb (%)	58.5 \pm 21.8	54.3 \pm 29.8
Correction of pelvic obliquity (%)	68.5 \pm 51.9	64.1 \pm 51.8
Minor complication (%)	17.5	25
Major complication (%)	8.8	20.8
Complication rate (%)	26.3	37.5

Table 6 List of complications 81 patients.

Major complications	
Part of drainage left in pleural cavity	1
Deep infection	3
Pneumonia	1
CVK induced septicemia	1
Crista screw problem leading to removal	2
Pseudoarthrosis	1
Progression outside fusion	1
Total complications	10 (12.3%)

1.5.2 Study II

The baseline data were comparable between the departments. H1 tended to have more patients of female gender, wheelchair bound, with diagnosis of spina bifida, and required more neurosurgical intervention (**Table 7**) therefore statistical analysis was performed with adjustment for the differences between groups using multiple regression.

- There was no peri- nor postoperative mortality. There was no spinal cord damage nor early or late neurological deterioration. The ambulatory function did not deteriorate in any case (Table 10).
- The rate of complications rendering to any intervention was 15.4%. Their distribution

between departments is given in **Table 10**.

- The mean loss of correction was 2 degrees during the follow-up.
- There were statistically significant between-department differences: mean deformity correction percentage was higher at H1 (Table 8)
- surgery time was shorter at H1 (Table 9)
- infections were more frequent at H2 ($p=0.04$; 6/65 at H1; 16/71 at H2) (Table 10)
- there was a tendency ($p=0.06$) of more department related complications at H2

Table 7 Demographic and baseline characteristics of groups.

MMC –Meningomyelocele, CP- Cerebral Palsy, SMA- Spinal Muscular Atrophy, Neuroendocrine-syndromes such as Rett syndrome.

	Total study group n=136	H1 n = 64	H2 n = 72
Age in years n \pm SD	12.1 \pm 5.5	11.5 \pm 6.8	12.7 \pm 4
Female n (%)	68 (50)	27 (42.2)	41 (56.9)
Number of fused segments n \pm SD	12.9 \pm 3.6	12.9 \pm 4.2	12.9 \pm 2.9
Curve size (Cobb $^{\circ}$) \pm SD	59.14 \pm 29.1	59.8 $^{\circ}$ \pm 32.2	58.5 $^{\circ}$ \pm 26.1
Functional status n (%)			
Full ambulators	20, (14.7)	10 (15.6)	10 (13.9)
Ambulators with neurologic disease	10, (7.4)	4 (6.3)	6 (8.3)
Ambulator with crutches and/or orthotics	20, (14.7)	6 (9.4)	14 (19.4)
Wheel-chair bound	86, (63.2)	44 (68.8)	42 (58.3)
Diagnosis n (%)			
MMC	29, (21.3)	17 (26.6)	12 (16.7)
CP	29, (21.3)	15 (23.4)	14 (19.4)
Duschenne	6, (4.4)	1 (1.6)	5 (6.9)
SMA	12, (8.8)	5 (7.8)	7 (9.7)
Neuroendocrine	12, (8.8)	6 (9.4)	6 (8.3)
Tumor related	29, (21.3)	11 (17.2)	18 (25.0)
Congenital	19, (14)	9 (14.1)	10 (13.9)
Procedures n (%)			
Anterior procedures	89, (65.4)	44 (68.8)	45 (62.5)
Neurosurgical intervention	34, (25)	19 (29.7)	15 (20.8)

Table 8 Radiographic variables, mean (\pm SD) for H1 and H2 before and after surgery. p= p-value of the difference in correction percentage between H1 and H2 adjusted for baseline differences between groups using multiple logistic regression, TK = thoracic kyphosis, LL= lumbar lordosis, PO pelvic obliquity

	Preop °		Postop °		Postop Mean correction %		p
	Mean (\pm SD)		Mean (\pm SD)				
	H1	H2	H1	H2	H1	H2	
Cobb	60 \pm 32	58 \pm 26	20 \pm 19	30 \pm 20	66	50	<0.001
Rotation	28 \pm 22	25 \pm 17	13 \pm 13	15 \pm 12	48	33	0.01
TK	22 \pm 38	36 \pm 21	26 \pm 18	31 \pm 13	64	62	0.98
LL	19 \pm 53	35 \pm 30	35 \pm 19	38 \pm 16	58	60	0.71
PO	16 \pm 15	7 \pm 10	3 \pm 7	3 \pm 4	58	29	0.003
Total for the study group							
Cobb	59 \pm 29		25 \pm 20		57		
Rotation	26 \pm 19		14 \pm 13		40		
TK	29 \pm 31		29 \pm 16		63		
LL	27 \pm 43		36 \pm 17		59		
PO	11 \pm 13		3 \pm 6		42		

Table 9 Length of surgery, intensive care unit (ICU) and hospital stay, and relative bleeding for total study group and according to departments.

*p-value of the difference between H1 and H2 adjusted for baseline differences between groups using multiple logistic regression.

Operative outcome, mean	Total study group n=136	H1 n=65	H2 n=71	Difference	95% Confidence interval of the difference	p value *
Surgery time (min)	535	498	572	74	-145.8, -1.6	0,01
ICU stay (days)	1,6	1.7	1.5	0.2	-0.15 , 0.7	0,39
Hospital stay (days)	11,6	12.5	10.8	1.7	-1, 4.4	0,25
Relative bleeding (%)	73	80.3	66	14.3	-2,2, 30.8	0,13
Correction of Cobb angle (%)	57,9	66.5	50.4	16.1	8.1, 23.7	<0.001

Table 10 Complications according to departments.

Complications	H1 n=65 n (%)	H2 n=71 n (%)	p value**
Hospital related complications*			
Part of drainage left in pleural cavity during removal	0(0)	1(1,4)	
Deep infection	2(3,1)	5(6,9)	
Pneumonia	1(1,6)	3(4,2)	
CVK induced septicemia	0(0)	1(1,4)	
Total	3(4,7)	10(13,9)	0,06
Surgical procedure or implant related complications			
Prominent crista screw, removal operation	4(6,3)	1(1,4)	
Other implant related problems, removal operation	1(1,6)	0(0)	
Pseudarthrosis	0(0)	1(1,4)	
Progression outside fusion	1(1,6)	0(0)	
Total	6(9,4)	2(2,8)	0,17
Total complications (15,4%)	9 (14,1)	12(16,7)	0.48
All infections(within major and minor complications)	6(9,4)	16(22,2)	0,04

* events not related to surgical procedures or implants.

** p value calculated adjusted for the baseline data differences (gender, diagnosis MMC, wheel chair bound and neurosurgery performed)

1.5.3 Study III

1.5.3.1 Comparison between controls and patients

1. *Position of pelvis: obliquity, inclination and rotation.* The 3D position of pelvis was described by set of three angles (**Figure 5/a,b,c**). The inclination was significantly smaller in patients ($p < 0.001$). The obliquity and rotation showed no significant differences. There was a statistically significant correlation ($p = 0.04$) between pelvic obliquity measured opto-electronically and radiographically.
2. *Position of thorax-shoulder complex: flexion, lateral bending and rotation.* The 3D position of thorax was described by set of three angles (**Figure 5/d,e,f**). There were no significant differences between patients and controls. All control subjects sat in a slightly more forward flexed position than the patients.
3. *The plumb line of C7 over S1.* The shoulder line did not follow the pelvis in the patient group in rotation, as opposed to the control group. This difference was significant ($p = 0.024$). No significant between-group differences were found in frontal and sagittal plumb lines. The frontal plane plumb line values in control subjects were consistent, ± 2 cm except 2 outliers. The sagittal plumb line values were similar in control and patient groups. The thoracic geometric centre was located 4 cm in front of the pelvic geometric centre (**Figure 5/g,h,j**).
4. *Seat load symmetry – right and left side.* There were statistically significant differences between the control and patient groups ($p = 0.04$) regarding seat load symmetry (**Figure 6/a**). Deviations up to 30% were recorded in the patient group. Variation in the control group was small, less than 7%.
5. *COP position symmetry- the β angle.* The symmetry of position of GRF vectors between left and right side was statistically significant ($p < 0.001$) (**Figure 6/b**). Statistically significant association was not found between beta angle and loading asymmetry in the patient group.
6. *Common COP position and symmetry in anterior-posterior and medial-lateral directions.* The location of Common COP relative to inter-trochanteric midpoint was more anterior in controls than in patients with a tendency to differ ($p = 0.06$). The medial-lateral asymmetry was similar between groups ($p = 0.46$) with a larger distribution in the patient group. (**Figure 6/c&d**)

1.5.3.2 Pre- and postoperative analysis

Four patients were accessible for postoperative analyses. Due to the low number of subjects only a descriptive analysis was possible on a case-to-case basis. In one case, a force platform had technical problems not observed until later. Thus, there are four postoperative kinematic and three postoperative kinetic analyses.

The pelvic obliquity was reduced in all 4 cases when measured using x-ray. The same information was possible to show with the present technique – in all three cases the obliquity was reduced to less than three degrees deformity. Pelvic tilt has changed towards more flexed position, but rotation position was similar before and after surgery.

Thorax position increased into flexion in 2 out of 4 cases, others stayed unchanged. The lateral bending changed within 10 degrees margin in one case. Thoracic rotation improved

considerably within 25 degrees margin in one case.

The C7 to S1 plumb line has deteriorate in 3-4 cm margin in two cases despite improved pelvic position and more symmetric seat loading. The seat loading beta angle value improved in 3/3 cases. The COP position became more anterior in 2/3 cases, medial - lateral COP position improved in 2/3 cases.

Figure 5 Pelvic tilt, obliquity and rotation in degrees with respect to the lab coordinate system. (a,b,c)

Thorax angular position in degrees with respect to the lab coordinate system in three planes. (d,e,f)

The plumb line of c7 over s1 in rotation (degrees), sagittal (dx, cm) and frontal planes (dz, cm). (g,h,i)

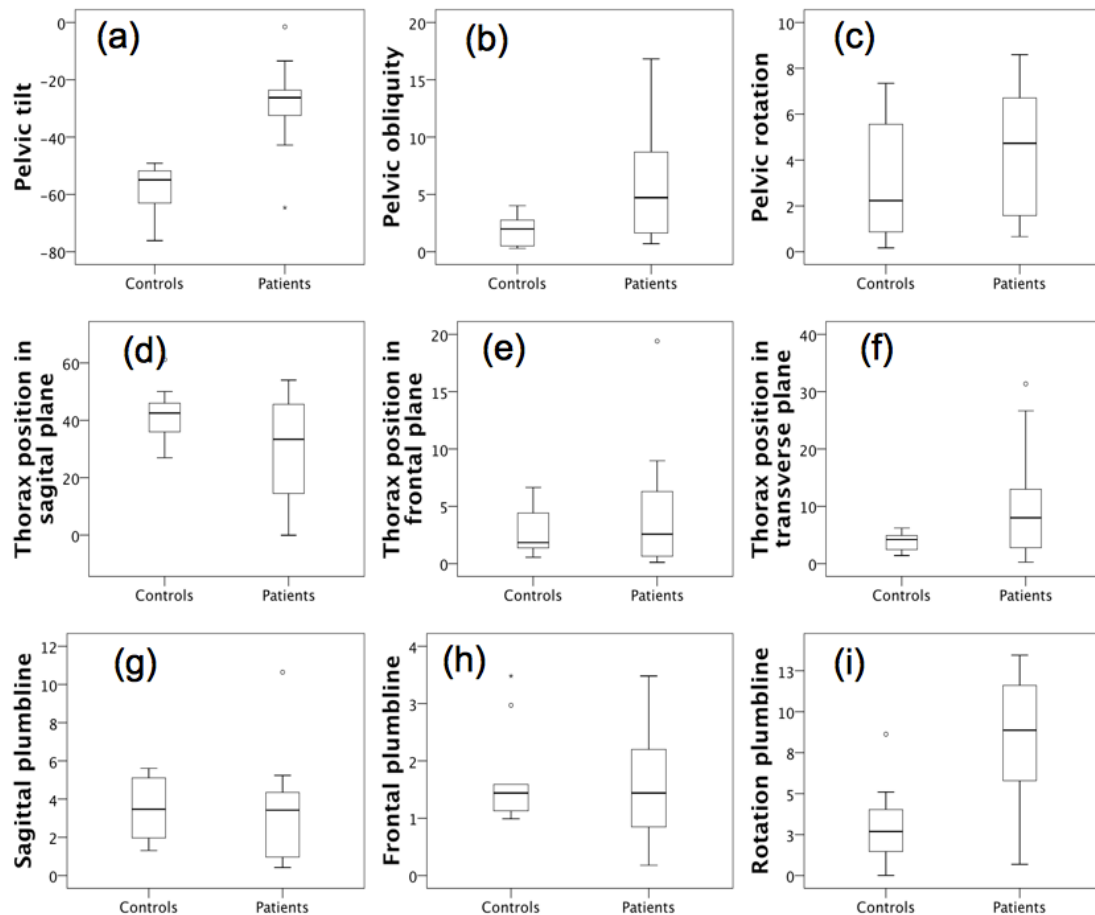
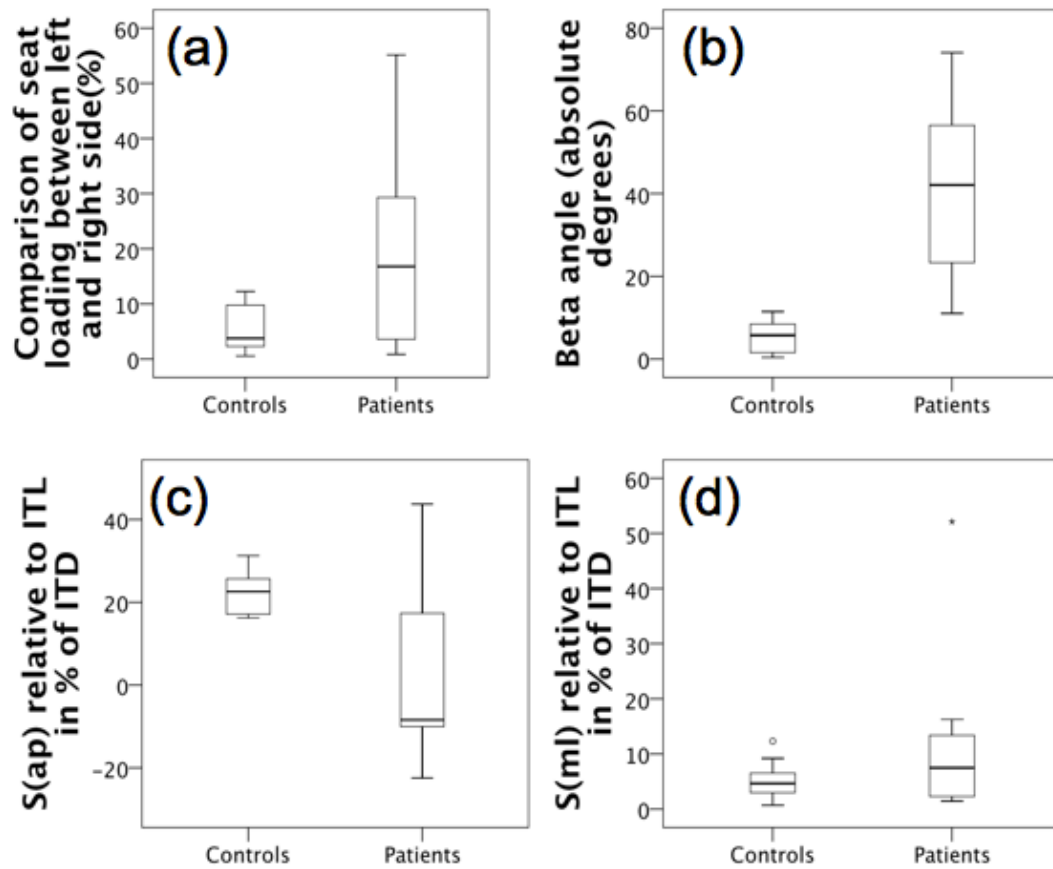


Figure 6 (a) The loading asymmetry index in percent in control and patient groups, (b) the asymmetry of COP position – The absolute β angle, (c) and (d) COP location in anterior-posterior direction S_{AP} and symmetry in medial-lateral directions S_{ML} .



1.5.4 Study IV

1.5.4.1 Comparison between controls and patients

The relative areas of the trajectories made by head and thoracic segments for the control group were significantly larger than for the patient group (757% vs. 209% of PBOS for head segment and 537% vs. 196% of PBOS for thoracic segment). The positional centroids of thorax-shoulder and head segment from the pelvic segment centre were not statistically different between groups. (**Figure 7/A&B**)

While the ACOP was larger in controls than in patients ($69 \pm 24\%$ vs. $51 \pm 69\%$, **Figure 7/C**), this difference was not statistically significant ($p=0.07$). The medial-lateral positional centroid of the COP was not significantly different between groups ($5 \pm 2.5\%$ of ITD for controls vs. $40 \pm 60\%$ of ITD for patients).

Loading /unloading index was statistically different between groups. The maximum range between loading of one force platform and unloading of opposite platform was in average 82% for controls comparing with 57 % of body weight for patient group. (**Figure 7/D**) The average loading of force platforms had a tendency ($p=0.07$) to be different between groups - control group had $7 \pm 6\%$ of BW difference compared to $14 \pm 9\%$ of BW in patients.

The association analysis revealed moderate association between force plate loading/unloading range and head trajectory area ($r=0.59$, $p=0.008$). Strong association was found between the area of head and thoracic trajectories ($r=0.96$, $p<0.001$) as well as loading/unloading range and COP area ($r=0.79$, $p<0.001$). A moderate association was found between area of COP and both area of head and thoracic trajectories ($r=0.59$, $r=0.008$ and $r=0.58$, $p=0.009$)

1.5.4.2 Pre and postoperative analysis

Four patients were available for postoperative analyses. Due to the low number of subjects only a descriptive analysis is presented on a case-to-case basis (**Figure 8**) In one case, a force platform had technical problems not observed until later. Thus, there are four postoperative kinematic and three postoperative kinetic analyses. ACOP increased in 3/3 patients with available kinetic data, the area of head and thoracic positional centroid trajectories increased in 4/4 and 3/4 patients, respectively. The loading/unloading index improved in 2/3 cases with available kinetic data. In 4/4 and 2/4 cases respectively the positional centroids of head and thoracic segments were located closer to the pelvic centre location in transverse plane. Symmetry of loading improved in 1/3 case and did not changed in 2/3 cases. The location of COP positional centroid point S_{AP} and S_{ML} did not revealed improvement of Symmetry of COP excursions in 2/3 cases.

Figure 7 The boxplots illustrating statistical comparison of patient and control groups (A) the area of head segment center trajectory in per cent of PBOS, (B) the area of thorax segment center trajectory in per cent of PBOS, (C) The area of COP excursions in per cent of PBOS, (D) Loading/unloading range in per cent of BW

PBOS – pelvic part of base of support, **BW** – body weight, **COP** – center of pressure

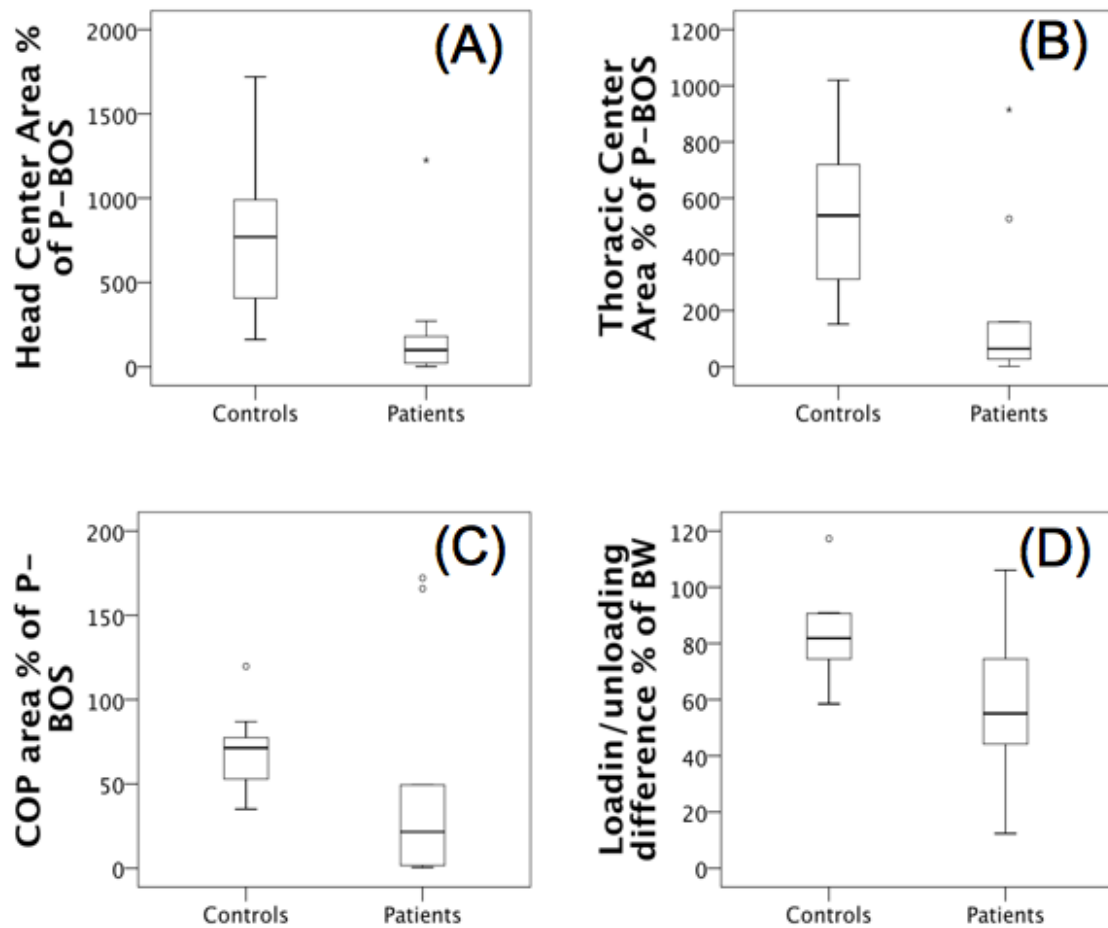
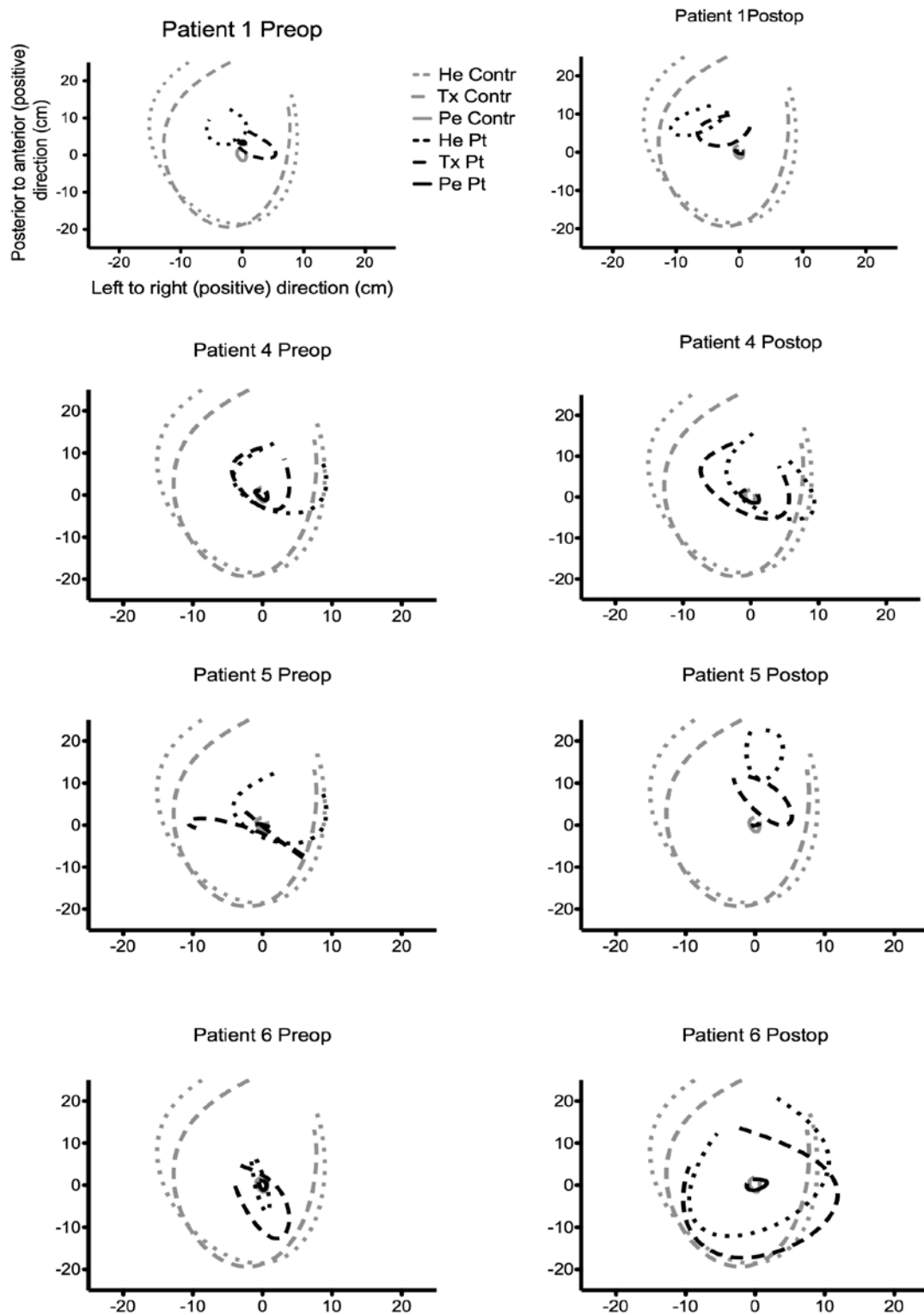


Figure 8 The case-to-case illustration of head, thoracic and pelvic segment trajectory analysis of pre/postoperative data measured in absolute distance in centimetres. 0,0 point is set on central calculated marker of pelvis. Grey lines designate mean trajectories of head, thorax and pelvis segments for control group.



1.6 DISCUSSION

1.6.1 Study I and II

To stabilize and straighten a collapsing spine in a patient with progressive deformity and to treat symptom- causing intra-spinal pathological conditions is not controversial^{24,25,27,40,86-91}. However, in the following circumstances an analysis of available possibilities to shorten the total treatment and rehabilitation time is of interest: 1) when the patient has multidisciplinary medical problems and high risks for serious complications; 2) when the surgery is complex and has to be individualized; and 3) when health care resources are restricted. It also can be questioned if any standard spine unit can treat these patients or if more specialization is needed, in particular in paediatric cases.

The overall complication rate at surgery for neuromuscular spine deformities is reported to be very high: 30%–90%, including implant-related problems, pseudarthrosis, loss of correction, and infections as well as death⁸⁷. Spina bifida -related deformities in particular are associated with high complication rates⁹²⁻⁹⁶. Contradictory documentation of the benefits of 1-stage versus multistage procedures exists^{88,97-101} with evolving recent trend to minimize indications for anterior approach^{102,103}. The loss of correction - not only as a measure of Cobb angle but including the rotation and pelvic parameters, in spite of a long follow-up time and skeletally immature cohort, was negligible. It can be hypothesized that the combined anterior procedure enhances the fusion and the stability of the reduction in cases with poor posterior tissues. In studies I and II, the overall complication rate corresponds to the lower rate of earlier reports, despite a selected patient population with the highest risk factors. There were no perioperative deaths or neurological complications. The loss of correction during follow-up was negligible, and only 1 case of pseudarthrosis could be identified. The 1-stage anterior and posterior procedure was safe. The addition of a neurosurgical procedure in the same session did not increase the risk of complications or the use of resources.

The comparison between the two departments showed differences regarding the occurrence of complications, wound infections in particular, as well as the length of the surgery time and correction percentage. H2 had more infections and other major complications, longer surgery time, and less deformity correction despite standardizing for surgeon, diagnosis, indication, and implant. H1 had longer follow-up time and earlier learning curve for implants usage, still better outcome and fewer infections including the late ones.

There were differences in the working routines between both the operation rooms and between the wards, difficult to quantify, nonetheless. At H1, individually tailored approach according to the diagnosis of the patient was practiced. Patients were seen peri-operatively by trained nurses and paramedical personnel, and other experts according to the patient specific needs. Paediatric specialists, such as neurosurgeon, neuro-radiologist, pulmonologist, and urologist were proactively involved. At H2, the local routines for standard adult spine surgeries were followed without making exceptions for paediatric cases. Consultation routines were restrictive and practiced only with written referrals. The anaesthesia personnel and scrub nurses had a special training for complicated paediatric cases at H1 contrary to H2.

The causes for differences between H1 and H2 can only be hypothesized. Risk for complications

have been studied from diagnosis/disease perspective, but the possible impact of work organization is also worth analysing due to its documented importance in other production fields^{35,36,104}. The workplace training and focus on special paediatric needs as well as proactive attitude being higher at H1 may have an important role on the outcome. These results request further studies on the impact of work organization and of workplace culture on the results of complex surgery.

The current project ran over a long time period, which might include confounders - data from H1 was included during 8 years, whereas H2 during 5 years. Also possible differences at baseline may have confounded results. However, the same surgeon, who followed a treatment program in cooperation with the neurosurgeon, performed all the deformity correction surgeries. Data were prospectively captured and all consequently included cases were followed up for 2 or more years. The baseline data were comparable between the groups and largest differences, although not statistically different, was adjusted during statistical analysis.

1.6.2 Study III and IV

The focus of studies III and IV, which were complementary analysis of quiet and dynamic sitting, was primarily methodological. To my knowledge, this is the first attempt to tailor and perform simultaneous kinetic and kinematic analyses on sitting in a patient group with motor and cognitive disabilities.

1.6.2.1 *Quiet sitting (study III)*

The seat load symmetry measurements with double force plates instead of the more common single force plate enabled us to identify significant differences between controls and patients which also has been demonstrated with pressure distribution techniques^{48,52,53,55}. Introduction of the β angle for COP symmetry analysis gives additional information to loading asymmetry measurements - association analysis did not reveal statistically significant relationship between them. The role of asymmetric and more anteriorly located GRF vector unilaterally in sitting stability and progression of deformity is to be evaluated in further studies.

As suggested already by Kylfoile¹⁰⁵ and also by Smith and Emans⁵² COG/COP (COP and COG practically coincide if there is no acceleration of the body as in still sitting^{5,64}) during unsupported sitting must lie well contained between both trochanters to ensure best equilibrium position for the body. Therefore common COP alignment analysis can be informative about quality of the sitting. COP_{common} symmetry analysis showed more anterior location for control subjects comparing with patients. The possible reasons for that might be the status of hip joints, which was not analysed. Medial -lateral symmetry of COP_{common} was not significantly different between patients and controls which indicates good postural control compensation of spinal deformity induced disequilibrium in the spine despite underlying neuromuscular disease.

In the kinematic domain of the analysis fewer statistical differences were found. When comparing the pelvic obliquity data from kinematics with x-rays, a good association was observed.

The four patients tested postoperatively improved after surgery. The seat loading became more

balanced and the COP in the separate force platforms equalized. Smaller changes were observed in kinematic domains. It seems that patients despite pelvic obliquity and load asymmetry tend to maintain their upper body balance during sitting. Therefore changes after surgery were smaller. Patients without any sitting balance before surgery were not included in this study.

1.6.2.2 Stability analysis (Study IV)

As expected, the sitting stability was obviously limited in the patient group as compared to normal controls. However, it was possible to carry on the tests on the current patient group in spite of their severe disabilities. Earlier methods have relied on the ability to actively perform coordinated upper extremity and hand movements, like reaching and moving an object. This particular function may often be impossible for patients with severe neuromuscular diseases, such as muscular dystrophies, spastic or flaccid paralysis including upper extremities, and congenital defects as well as in cognitive function deficiencies. Thus, the current method makes a larger patient group available for studies on sitting function including a quantitative documentation, which is a prerequisite for future improvements.

The results in able-bodied controls were consistent and showed small variation, whereas the results of the patient group diverged and differed clearly from the able-bodied. Thus the method is able to differentiate and document pathological findings. The postoperative analyses, though few, show that the method has some potential to quantitatively describe and analyse treatment-dependent changes over time. These promising results of the feasibility study warrant future studies on larger patient groups. The technique still requires some degree of cooperative ability, particularly during marker placement and motion data collection.

There were differences between patients and controls in both segment trajectories and COP trajectories of the FLS. There was a good agreement between these trajectory analyses. These findings are in accordance with few previous studies with some similarities in study design^{67,106}. It can be questioned whether segment and COP trajectories can be used interchangeably. In our opinion the two measurements are tightly connected, but the COP signal has a postural control origin^{5,64}, whereas upper body segment trajectory is a direct reflection of body movements. They are rather complementary methods to measure postural stability.

As a group, the patients did not differ significantly from controls in symmetry of movements using a trajectory assessment. A closer case-to-case observation could depict distinct cases of major asymmetry in segment trajectories. The value of such trajectory assessment as a preoperative evaluation tool in conjunction with classical balance assessment modalities should be analysed further.

The double force platform strategy gives important information on seat load asymmetry and worked as well in the dynamic analyses as in static analyses of earlier studies^{55,73,80,83}. It seems to be a promising tool to evaluate the surgical outcome in spine deformity cases with pelvic obliquity.

1.6.2.3 Limitations for study III and IV

The studies have several limitations. There are no standard marker setups to use in the analysis of kinematics in sitting. Our marker setup had some drawbacks: comparing with gait analysis marker setups leg markers and anterior chest wall markers were not used due to identification problems by the opto-electronic detection system and an attempt to keep the

evaluation time short. The marker position can be studied further.

The small sample size and lack of postoperative follow-up of 10 (study III)/ 6 (study IV) patients precludes us from generalizing the results of the study. The methodology, furthermore, still requires some level of cooperativeness, particularly during marker placement and motion data collection

1.7 CONCLUSIONS

1.7.1 Study I and II

The clinical tradition at most treatment units is to perform neurosurgical and orthopaedic procedures separately. Medico-legal issues might contribute to this practice. According to the current study, it is safe to perform major spine deformity surgery in high-risk patients with complex morbidity in one session – also including a neurosurgical intervention if indicated. It saves resources and rehabilitation time. The complication rate can be kept at an acceptable level and the correction is lasting. Factors for further decrease of complication rate were identified. In addition to medical patient parameters, workplace culture and organization may have an impact on treatment results.

1.7.2 Study III and IV

The present model of simultaneous kinetic and kinematic analyses is applicable in patient groups with motor disabilities and inferior cognitive ability. The method adds valuable quantitative information to document the pathology and intervention dependent changes. During a short sitting session, patients with neuromuscular spine deformities were able to keep a balanced upper body position and COP location relative to pelvic midpoint despite distorted pelvic position, seat load asymmetry and asymmetrically positioned GRF vectors. Postural compensation is worth further studies.

The presented dynamic kinetic and kinematic method is a promising quantitative measurement tool for comparisons of sitting function, both inter-individually between groups and intra-individually over time. It is able to provide objective analysis to follow up the outcome of interventions in disabled patients with major spine deformity, pelvic obliquity and severe problems of body alignment.

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